EXTENDED REPORT

Histological parameters helpful in recognising steroid-treated temporal arteritis: an analysis of 35 cases

Ramon L Font, Venkatesh C Prabhakaran

Br J Ophthalmol 2007;**91**:204–209. doi: 10.1136/bjo.2006.101725

See end of article for authors' affiliations

Correspondence to: Dr R L Font, Ophthalmic Pathology Laboratory, Cullen Eye Institute, Baylor College of Medicine, One Baylor Plaza, Houston, Texas 77030, USA; rfont@bcm.tmc.edu

Accepted 13 September 2006
Published Online First 20 September 2006

Aim: To establish the histological and immunohistochemical parameters that are helpful in recognising temporal arteritis in patients who have been treated with steroids before biopsy, and to analyse the clinical features and correlate them with the histological findings.

Methods: A retrospective review of charts of 35 patients treated with steroids before obtaining temporal artery biopsy specimens, spanning a 11-year period from 1995 to 2005. The study was conducted at the Ophthalmic Pathology Laboratory, Cullen Eye Institute, Houston, Texas, USA. The clinical features were evaluated and correlated with the histopathological findings. Each case was evaluated with respect to age, sex, race, clinical findings, erythrocyte sedimentation rate, corticosteroid dosage (oral versus intravenous) and the duration of treatment. The time interval between obtaining the biopsy specimen and the onset of steroid treatment was carefully recorded for each patient. In selected cases, histiocytic markers (CD-68 and HAM-56) were used to identify the presence of epithelioid histiocytes, which characterises a granulomatous inflammation. Other immunohistochemical studies (CD3, CD20, CD4, CD8, CD45RO, CD45RA and S-100 protein) were performed in selected cases to characterise the inflammatory cells.

Results: The three most reliable histopathological parameters of corticosteroid-treated temporal arteritis are the following: (1) complete or incomplete mantle of lymphocytes and epithelioid histiocytes located between the outer muscular layer and the adventitia; (2) large circumferential defects in the elastic lamina (best seen with the Movat's pentachrome); and (3) absent or few small multinucleated giant cells. In some cases the main artery appears normal, whereas the primary branches show evidence of a healing arteritis. The histological findings vary according to the duration of treatment before obtaining the biopsy specimen.

Conclusion: Striking histological differences can be recognised objectively between patients with active (untreated) giant cell arteritis and patients who have been treated with corticosteroids. The earliest histopathological changes were detected by the end of the first week after steroid treatment (usually after day 4 to the end of the first week). The histological findings were more difficult to recognise at 2–3 months after steroid treatment. Ophthalmic and general pathologists should be able to recognise this entity on the basis of the histological findings including the special stains and results of immunohistochemical studies (CD-68 and HAM-56).

Temporal arteritis or giant cell arteritis (GCA) is a vascular disease characterised by a granulomatous panarteritis of medium-sized arteries. The inflammation often appears clinically to be limited to the cranial arteries, with involvement of the temporal arteries.[1 2] The mean (standard deviation (SD)) age of patients with temporal arteritis is 75.2 (5.0) years.[3]

The disease is characterised by fever, headaches, visual impairment, scalp tenderness, malaise, myalgia, weight loss, anaemia, jaw claudication, neck pain and tenderness of the temporal artery to palpation with decreased arterial pulsation among other less specific symptoms. Usually, the erythrocyte sedimentation rate is increased. The onset of symptoms rarely occurs before 50 years of age (median is 70 years), with a clear predilection for women.[4] The dreaded complication of temporal arteritis is blindness. The best treatment for this disease is early diagnosis followed by prompt treatment with corticosteroids.

Although laboratory tests (erythrocyte sedimentation rate, C-reactive protein, platelet count) are commonly done while investigating a patient with suspected temporal arteritis,[5] the gold standard for diagnosis is histological confirmation of temporal artery biopsy specimens.

The purpose of this study was to analyse the histopathological parameters that are helpful in recognising healing temporal arteritis after steroid treatment.

MATERIALS AND METHODS

We reviewed the records of all temporal artery biopsy specimens on file in the Ophthalmic Pathology Laboratory, Cullen Eye Institute, Baylor College of Medicine, Houston, Texas, USA, during a 11-year period (1995–2005). Clinical information and follow-up data were analysed when available. Records of those patients with a positive temporal artery biopsy who were treated with steroids before the biopsy specimens were collected and analysed. The diagnosis of temporal arteritis was made if an inflammatory infiltrate containing both lymphocytes (mononuclear cells) and epithelioid histiocytes was detected in the arterial wall. A total of 35 cases were found. The length of the temporal artery submitted for histopathological interpretation was also recorded along with the results of erythrocyte sedimentation rate and the demographic features (age, sex and race). The dosage and duration of steroid treatment were recorded for each case. All the biopsy specimens were fixed in 10% buffered formaldehyde solution, then sectioned in multiple 1-mm segments with a razor blade and embedded using the agar technique.[6] Four micra sections were stained with haematoxylin-eosin, periodic acid Schiff, Movat's pentachrome and the Masson's trichrome methods. The slides were reviewed in all cases, and the histological findings recorded on a diagrammatic template used for temporal artery biopsy specimens. In 10 selected cases, histiocytic markers (CD-68 and HAM-56) were used to identify epithelioid histiocytes that characterise a granulomatous inflammation. Levels of immunological markers for T and B-cells (CD3, CD20, CD4,

Abbreviations: GCA, giant cell arteritis

CD8, CD45RO, and CD45RA) and S-100 for dendritic cells were determined in five selected cases to identify the nature of the inflammatory cells.

The 35 cases were further subdivided into groups on the basis of the duration of steroid treatment: ⩽5 days, 6–14 days and >14 days, and a subgroup analysis was performed in an attempt to correlate the histological findings and the duration of corticosteroid treatment. In addition, the histological features of the patients treated with intravenous methylprednisolone were compared with those of patients treated with oral steroids for a comparable duration.

RESULTS

Tables 1 and 2 gives the summary of the clinical and demographic data. Clinical symptoms were consistent with those previously described for giant cell arteritis.

Histopathological findings

All the 35 cases showed the following histological features:

- A mantle of lymphocytes mixed with mononuclear cells and epithelioid histiocytes, located at the junction of the outer muscle layer and the adventitia. (figs 1, 2)
- Loss of the internal elastic lamina, usually 40–50% of the circumference of the artery, best seen with the Movat pentachrome stain.

In addition, the following features were observed:

- A more diffuse inflammatory infiltrate involving the muscle layer and the adventitia, in addition to the band-shaped infiltrate at their junction, was observed in 18 of 35 cases, especially in those with a very short duration of steroid treatment.
- Giant cells were seen in 15 of 35 cases. They were usually sparse and sometimes seen only on serial sectioning of the biopsy specimen (fig 3).
- In 4 of 35 cases, the arteries exhibited a thick mantle of postnecrotic scarring of the media that was outlined on both sides by a palisade of epithelioid cells and fibroblasts without multinucleated giant cells (fig 4).
- Involvement of small vessels (primary branches) adjacent to the main artery was observed in 8 of 35 cases.

Table 1 Summary of clinical and demographic data

Age range	60–87 years
Mean age	74.7 years
Sex	
Men	12 (34%)
Women	23 (66%)
Race	
Caucasian	32
African American	1
Unknown	2
Length of artery	7–35 mm (mean 16.6 mm)
Oral prednisolone dosage	30–100 mg/day
IVMP dosage	1000 mg/day
Duration of treatment	Variable from 3 to 90 days (mean 19.2 days)
ESR	22–134 mm/h (mean 66.7 mm/h)

ESR, erythrocyte sedimentation rate; IVMP, intravenous methylprednisolone.

- In many cases, a dense lymphocytic inflammatory infiltrate was noted around the vasa vasorum of the artery (24/35 cases).

The results of the subgroup analysis were as follows.

A total of 15 patients had been treated with steroids for <6 days (group 1), 11 patients in the 6–14-day group (group 2) and 9 patients in the >14-day group (group 3). All nine specimens in group 3 had inflammation limited to the media–adventitia junction, whereas 7 of 11 cases in group 2 and 11 of 15 cases in group 1 had additional diffuse infiltrates in the arterial wall.

Giant cells were present in 8 of 15 cases in group 1, 4 of 11 cases in group 2 and 2 of 9 cases in group 3.

Six cases treated with intravenous methylprednisolone (average duration of treatment: 4.5 days; average dose of steroids: 3103 mg) were compared with six cases treated with oral prednisolone for a comparable duration (average duration: 4.2 days, average dose: 313 mg). No obvious histological differences were noted between the temporal artery specimens from patients treated with intravenous methylprednisolone and those treated with oral steroids.

Immunohistochemical studies

CD-68 and HAM-56 were focally positive within the mantle of inflammatory cells in all sections of the artery in which they were studied (fig 5). Almost all the inflammatory cells were T cells (CD3 positive and CD20 negative). Further, all these cells were CD45RO positive (marker for memory T-cells, fig 6) and negative for CD45RA (marker for naïve T-cells, fig 7). In the cases studied, the CD4:CD8 ratio was almost equal, with a slight predominance of CD8-positive cells (figs 8, 9).

S-100-positive cells (dendritic cells) were present focally in the adventitia, in some areas adjacent to the clusters of epithelioid histiocytes (fig 10). The nerves in the adventitia serve as a positive control.

DISCUSSION

Our study strongly suggests that steroid treatment of patients with GCA causes marked changes in the histological features of the disease. It is critical for general and ophthalmic pathologists to recognise the histopathological parameters to minimise the false negative results of biopsy specimens. The occurrence of false negative biopsies may be the result of a focal involvement of the muscular arteries by the disease process (skip areas),[7 8] inadequate sampling for histological examination and the inability of the pathologist to recognise the histological changes described herein in treated cases of temporal arteritis. In our experience, skip areas[8] is an unusual finding, which has also been described by McDonnell *et al*.[9]

The most common histopathological features in steroid-treated temporal arteritis are:

- Mantle of lymphocytes and epithelioid histiocytes with pale cytoplasm and elongated to reniform nuclei mostly located at the junction of the outer muscle layer and adventitia. This has also been described by Schmidt and Loffler[10] and Achkar *et al*.[11]
- Rare multinucleated giant cells were seen in the mantle of inflammatory cells or localised adjacent to the elastic lamina.[10] They were more frequently observed in short-term steroid-treated cases and rarely in cases with long-term treatment.
- Large circumferential defects or complete absence of the elastic lamina have also been described.[9 12–16]
- The presence of postnecrotic scarring of the muscle layer bordered by a palisade of epithelioid histiocytes with diffuse adventitial thickening is less common.

Table 2 Clinical summary of 35 cases of steroid-treated temporal arteritis

Case	Length of artery (mm)	Eye involved	Age (years)	Sex	Race	ESR (mm/h)	Corticosteroid dosage (mg)	Duration of treatment (days)	Cumulative dose (mg)
1	16	OD	75	F	C	96	60	7	420
2	10	OS	76	F	C	100	30	3	90
3	15	OD	77	F	C	58	60	60	3600
4	9	OS	64	M	C	NK	60	45	2700
5	16	OD	60	F	C	134	60	5	300
6	21	OS	75	M	C	76	60	5	300
7	15	OD	82	F	C	100	40	42	1680
8	8	OD	86	F	C	110	60	16	220
9	20	OD	62	M	C	NK	100	3	300
10	23	OD	76	F	C	112	IVMP 1000	3	3000
11	31	OD	71	F	C	NK	60	90	5400
12	12	OS	63	F	C	115	100	4	400
13	15	OS	70	F	C	22	80	7	560
14	7	OD	75	M	C	99	IVMP 1000	3	3000
15	NK	OS	74	F	C	58	IVMP 1000	3	3000
16	10	OD	71	F	C	53	60	21	1260
17	12	OD	79	F	C	75	60	4	240
18	20	OD	68	F	NK	NK	IVMP 1000×3 days, 100 6 weeks, 80 2 weeks	60	8320
19	NK	OD	69	F	C	45	40×3 days, 80×3 days	6	360
20	35	OS	67	M	AA	NK	60	10	600
21	25	OD	76	M	C	115	80	5	400
22	NK	OS	66	F	NK	81	60	3	180
23	19	OD	74	F	C	6	60	7	420
24	14	OS	78	M	C	60	60	7	420
25	14	OD	80	M	C	49	Medrol dose 10 g pack 3 months before Bx	3	300
26	16	OS	87	M	C	10	200 IV×2 days 80×5 days		
	7	800							
27	16	OS	87	M	C	40	40×3 days 60×2 days		
	5	240							
28	18	OS	67	F	C	6	80	10	800
29	15	OD	74	M	C	38	100×6 days Medrol dose pack (150 mg total)		
	7	750							
30	15	OD	77	M	C	47	60	10	600
31	9	OS	82	F	C	12	5	180	900
32	13	OD	80	F	C	NK	IVMP 1000 mg×3 days 80	4	3080
33	19	OD	80	F	C	NK	40	12	480
34	22	OD	77	F	C	85	IVMP 1000 mg×3 days 80 mg×3 days		
	6	3240							
35	20	OD	89	M	C	NK	60×5 days, IVMP 1000 mg×3 days	8	3300

AA, African American; Bx, ; C, Caucasian; ESR, erythrocyte sedimentation rate; F, Female; IV, intravenous; IVMP, Intravenous methylprednisolone; M, Male; NK, not known; OD, right eye; OS, left eye

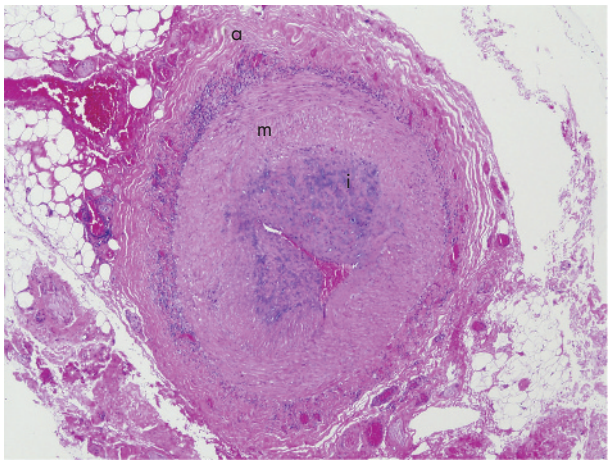

Figure 1 Low-power view of the temporal artery depicting intimal hyperplasia (i) with reduction of the vascular lumen. A band-shaped inflammatory infiltrate is seen at the junction of the muscle layer (m) and adventitia (a). Haematoxylin-eosin ×4.

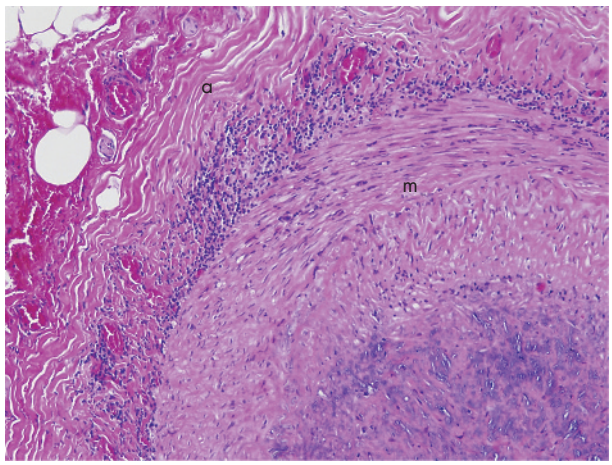

Figure 2 High-power view of fig 1 displaying the mantle of lymphocytes and epitheliod histiocytes between the media (m) and adventitia (a). No multinucleated giant cells are present. Haematoxylin-eosin ×20.

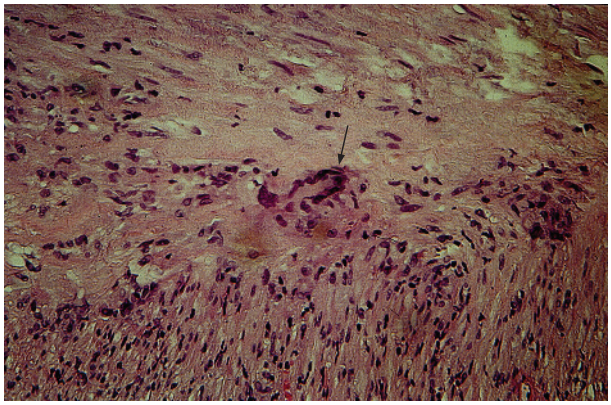

Figure 3 Section of an artery depicting a multinucleated giant cell (arrow). Haematoxylin-eosin ×40.

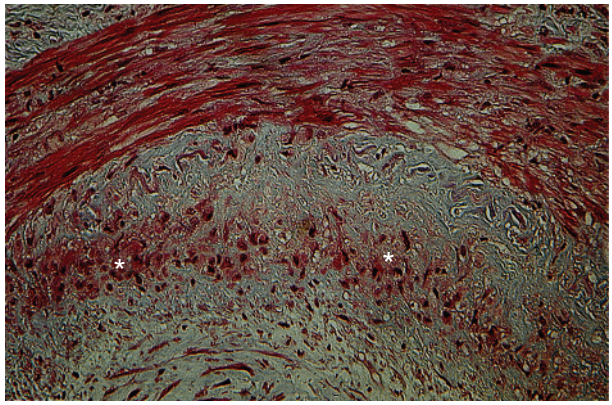

Figure 4 A high-power view showing a band of necrosis bordered by epithelioid histiocytes (asterisks). Masson trichrome ×40.

These changes are in contrast with the classic histological findings in temporal arteritis—namely, a diffuse granulomatous inflammatory infiltrate involving the entire arterial wall (panarteritis) but centred in the media, with disruption of the internal elastic lamina.

We believe that the percentage of false-negative biopsies can be minimised considerably by following the diagnostic criteria that we outlined above. We strongly recommend the use of special stains (Movat's pentachrome and Masson's trichrome) and immunohistochemical stains (CD-68 and HAM-56) in the histological analysis of the specimens. CD-68 seems to be more reliable than HAM-56 in identifying the epithelioid histiocytes. McAllison and Gallagher[13] suggested that, in corticosteroid-treated cases, the inflammatory reaction resolves quickly, both clinically and histologically. They suggested that the percentage of false-negative biopsies increases soon after initiation of corticosteroid treatment. Traditional teaching suggests that the temporal artery biopsies should be performed within the first week after beginning steroid treatment, to establish the correct histological diagnosis.[17]

Hall *et al*[18] suggested that the temporal artery biopsy specimen should be obtained from all patients before they are committed to long-term, high dose corticosteroid treatment. We are in agreement with the observations of Achkar *et al*[11] and Ray-Chauduri *et al*[19] that if clinical suspicion of giant cell arteritis is present, it is reasonable to perform a temporal artery biopsy to confirm if arteritis is present even in patients who have received previous corticosteroid treatment. Chmelewski *et al*[20] and Wells *et al*[16] believe that the administration of corticosteroids before the biopsy does not alter the histological results. Some authors considered that temporal artery biopsies should be performed in all suspicious cases, regardless of whether they had been previously treated with corticosteroids before the biopsy.[21 22] Obviously, there is quite a bit of controversy regarding the timing of when to perform a temporal artery biopsy after initiating corticosteroid treatment.

We also did not find a significant difference in histology between biopsy specimens from patients treated with oral steroids and specimens from those treated with intravenous methylprednisolone. The clinical relevance of this finding is uncertain.

The other interesting finding in our series is the significant number of cases with small vessel involvement (8/35 cases). Inflammation limited to the small vessels alone should prompt an investigation for small-vessel vasculitides such as Wegener's granulomatosis, but, in many cases of temporal arteritis, the small vessels adjacent to the main artery are involved, and this is a useful, if not often overlooked, finding.[23]

Results of the immunohistochemical studies in our cases are in keeping with those reported in previous studies. They support Weyand and Goronzy's hypothesis regarding the pathogenesis of temporal arteritis[24 25] (fig 11).

The exact mechanism of action of steroids in temporal arteritis is unknown. One of their primary modes of action, however, is by inhibiting nuclear factor κB and cytokines such as interleukin 6, whose genes are activated by nuclear factor κB.[24 25] This explains the reduction in the inflammatory infiltrate after steroid treatment. Steroids, however, have very little effect on interferon γ and do not influence the (unknown) antigenic stimulus. This may explain why all the residual T cells are CD45RO-positive memory cells. It also explains the need for prolonged corticosteroid treatment.

It is also interesting that we found the CD4:CD8 ratio to be almost equal, with a slight predominance of CD8. This is contrary to most other studies of temporal arteritis, where the inflammatory infiltrate is predominantly CD4. This increase in CD8 may be an unexplained effect of steroid treatment, which has been noted previously in one study.[26]

Our goal is to define histologically the entity of corticosteroid-treated temporal arteritis to provide uniform criteria for histological recognition of this entity. Our results are in agreement with the observations of McDonnell *et al*[8] and the diagnostic criteria which they outlined for ''healed arteritis''. However, in their study, they had a high rate of interobserver variation when making the diagnosis of healed arteritis. With

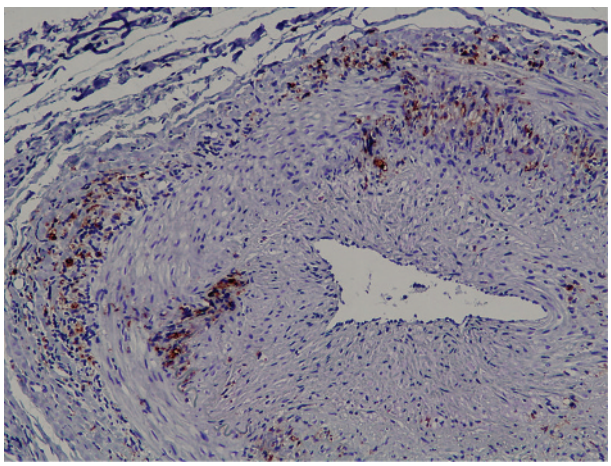

Figure 5 Section of artery showing CD-68-positive epithelioid histiocytes intermixed with lymphocytes (CD-68, ×20).

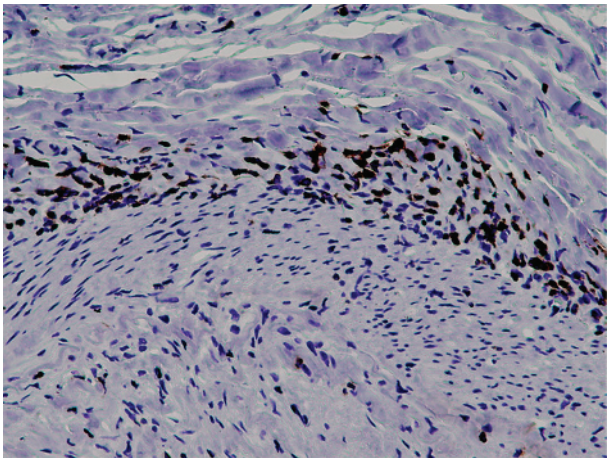

Figure 6 Immunostaining with CD3 (a T-cell marker) shows that almost all the cells in the band-shaped infiltrate are T cells. CD3, ×40.

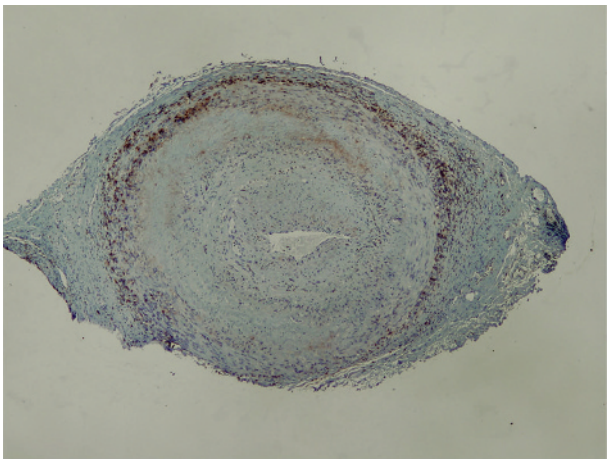

Figure 7 Low-power view of the artery showing the band-shaped lymphocytic infiltrate between the media and adventitia. The lymphocytes are immunoreactive for CD45RO, a marker for memory T-cells. CD45RO, ×4.

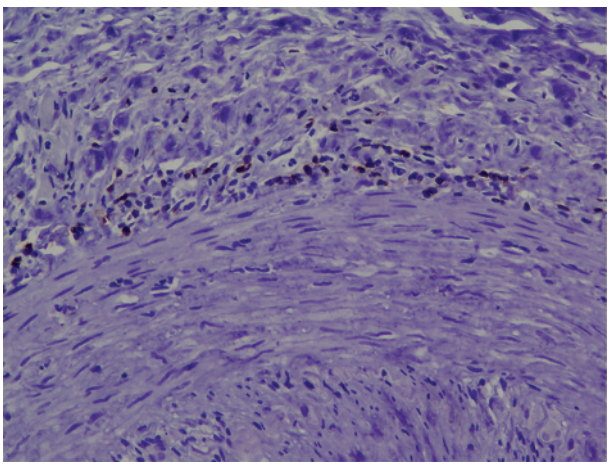

Figure 8 Immunostaining for CD4 (fig 3) and CD8 (fig 4) shows that the ratio CD4:CD8 is approximately 1:1 within the lymphocytic infiltrate. The CD8-positive cells appear to stain more intensely. CD4 and CD8, ×40.

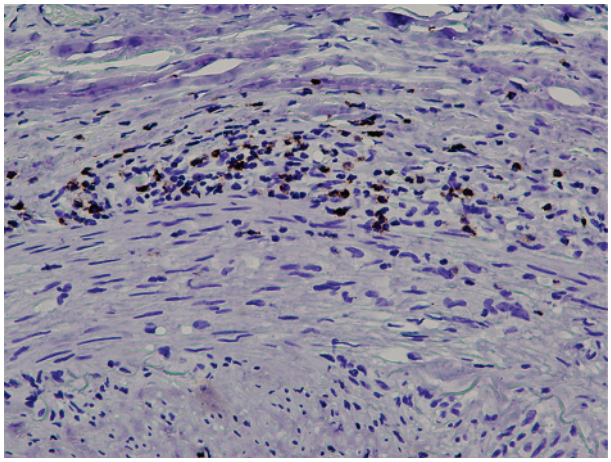

Figure 9 Immunostaining for CD4 (fig 3) and CD8 (fig 4) shows that the ratio CD4:CD8 is approximately 1:1 within the lymphocytic infiltrate. The CD8-positive cells appear to stain more intensely. CD4 and CD8, ×40.

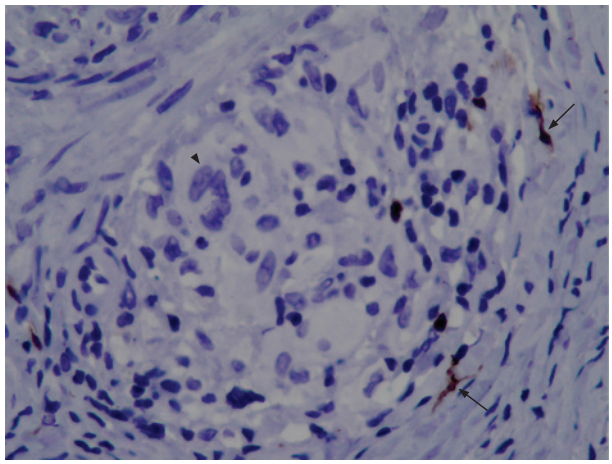

Figure 10 High-power view showing S-100-positive dendritic cells in the adventitia (arrows) in close proximity with a focus of granulomatous inflammation containing epithelioid histiocytes. A multinucleated giant cell is also seen (arrowhead; S-100 protein, ×40).

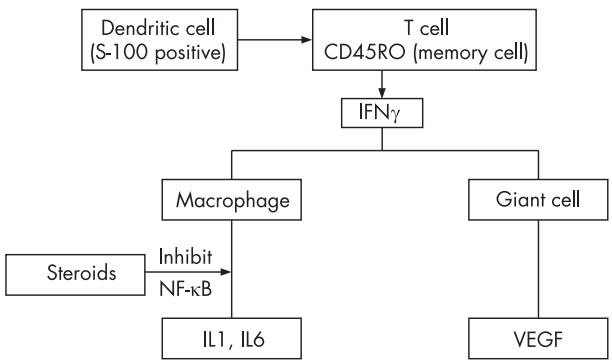

Figure 11 Pathogenetic mechanisms in giant cell arteritis (modified from Weyand and Goronzy[24 25]).

recognition of the histological features of corticosteroid-treated temporal arteritis, we hope that our findings will be confirmed by a larger, multicentre randomised study, comparing cases of typical giant cell arteritis with no history of steroid treatment with cases having had prior steroid treatment.

Striking histological differences can be recognised objectively between typical (untreated) cases of GCA and patients who have been treated with corticosteroids before the biopsy. We therefore strongly encourage clinicians to inform pathologists if patients have received steroids before biopsy, and to include details of the dosage and duration of treatment. We believe general and ophthalmic pathologists should be able to identify the differences on the basis of careful evaluation of the histological parameters and histochemical markers. Based on the results of our study, we also believe that it is reasonable to perform temporal artery biopsy, if clinically indicated, irrespective of the duration of prior corticosteroid treatment.

ACKNOWLEDGEMENTS

We thank Andres Garcia and Chetankumar B Patel for their help in the early stages of this project.

Authors' affiliations

Ramon L Font, Venkatesh C Prabhakaran, Department of Ophthalmology, Cullen Eye Institute, Baylor College of Medicine, Houston, Texas, USA

Funding: This study was supported in part by grants from the Retina Research Foundation, Houston, Texas, USA,and Research to Prevent Blindness, New York, New York, USA.

RLF is the recipient of the Senior Investigator Award from Research to Prevent Blindness, New York, New York, USA.

REFERENCES

1 **Healey CA**, Wilske KR. Temporal arteritis. *Med Clin North Am* 1977;**61**:261–5.
2 **Huston KA**, Hunder GG, Lie JT, *et al*. Temporal arteritis: a 25-year epidemiologic, clinical and pathology study. *Ann Intern Med* 1978;**88**:162–6.
3 **Liu NH**, LaBree LD, Feldon SE, *et al*. The epidemiology of giant cell arteritis: a 12-year retrospective study. *Ophthalmology* 2001;**108**:1145–9.
4 **Ettinger RE**, Hunder GC, Ward LE. Polymyalgia rheumatica and giant cell arteritis. *Annu Rev Med* 1978;**29**:15.
5 **Niederkohr RD**, Levin LA. Management of the patient with suspected temporal arteritis. A decision-analytic approach. *Ophthalmology* 2005;**112**:744–56.
6 **LoRusso FJ**, Font RL. Use of agar in ophthalmic pathology. *Ophthalmology* 1999;**106**:2106–8.
7 **Hedges III TR**, Gierger GL, Albert DM. The clinical value of negative temporal artery biopsy specimens. *Arch Ophthalmol* 1983;**101**:1251–4.
8 **Klein RG**, Campbell RJ, Hunder GC, *et al*. Skip lesions in temporal arteritis. *Mayo Clin Proc* 1976;**51**:504–10.
9 **McDonnell PJ**, Moore GW, Miller NR, *et al*. Temporal arteritis. A clinicopathologic study. *Ophthalmology* 1986;**93**:518–30.
10 **Schmidt D**, Loffler KU. Temporal arteritis, comparison of histological and clinical findings. *Acta Ophthalmol* 1994;**72**:319–25.
11 **Achkar A**, Lie JT, Hunder GG, *et al*. How does previous corticosteroid treatment affect the biopsy findings in giant cell (temporal) arteritis? *Ann Int Med* 1994;**120**:987–92.
12 **King WT**, Enzer YR, Tsiaras WG. Temporal artery biopsy after one month of corticosteroid therapy. *Am J Ophthalmol* 1994;**117**:265–7.
13 **Allison MC**, Gallagher PJ. Temporal artery biopsy and corticosteroid treatment. *Ann Rheum Dis* 1984;**43**:416–17.
14 **Brownstein S**, Nicolle DA, Codire F. Bilateral blindness in temporal arteritis with skip areas. *Arch Ophthalmol* 1983;**101**:388–91.
15 **Cohen DN**. Temporal arteritis: improvement in visual prognosis and management with repeat biopsies. *Trans Acad Ophthalmol Otolaryngol* 1973;**77**:74–85.
16 **Wells KK**, Folberg R, Goeken JA, *et al*. Temporal artery biopsies: correlation of light microscopy and immunofluorescence microscopy. *Ophthalmology* 1989;**96**:1058–64.
17 **Miller NR**. Temporal arteritis. In: Fraunfelder FT, Roy FH, eds. *Current ocular therapy*.3rd edn. Philadelphia: WB Saunders, 1990:170.
18 **Hall S**, Persellin S, Lie JT, *et al*. The therapeutic impact of temporal artery biopsy. *Lancet* 1983;**2**:1217–20.
19 **Ray-Chauduri N**, Kine DA, Tijani SO, *et al*. Effect of prior steroid treatment on temporal artery biopsy findings in giant cell arteritis. *Br J Ophthalmol* 2002;**86**:530–2.
20 **Chmelewski WL**, McKnight KM, Agudelo C, *et al*. Presenting features and outcomes in patients undergoing temporal artery biopsy. A review of 98 patients. *Arch Intern Med* 1992;**152**:1690–5.
21 **Wegener HP**, Hollenhorst RW. The ocular lesions of temporal arteritis. *Am J Ophthalmol* 1958;**45**:615–30.
22 **Fauchald P**, Rygrold O, Oystese B. Temporal arteritis and polymyalgia rheumatica: clinical and biopsy findings. *Ann Intern Med* 1972:845–52.
23 **Chiu CS**, Dryja TP, Lessell S. A ''negative'' temporal artery biopsy, positive for arteritis. *Arch Ophthalmol* 2004;**122**:1074–5.
24 **Weyand CM**, Goronzy JJ. Medium- and large-vessel vasculitis. *N Engl J Med* 2003;**349**:160–9.
25 **Weyand CM**, Goronzy JJ. Giant cell arteritis: pathogenesis. In: Hoffman GS, Weyand CM, eds. *Inflammatory diseases of blood vessels*. New York: Marcel Dekker, 2002, 413–23.http://www.ncbi.nlm.nih.gov.ezproxyhost.library.tmc.edu/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11407699&query_hl=4&itool=pubmed_docsum (accessed 6 Dec 2006).
26 **Cid MC**, Campo E, Ercilla G, *et al*. Immunohistochemical analysis of lymphoid and macrophage cell subsets and their immunologic activation markers in temporal arteritis. Influence of corticosteroid treatment. *Arthritis Rheum* 1989;**32**:884–93.